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| APPLICATION NO. | FILING DATE | FIRST NAMED INVENTOR | ATTORNEY DOCKET NO. |
|---|---|---|---|
| 07/784,222 | 10/28/91 | WESTBROOK C | ARCD:010/UCH |

18M2/0612

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REES, EXAMINER

| ART UNIT | PAPER NUMBER |
|---|---|
| 1807 | 19 |

DATE MAILED: 06/12/96

**Please find below and/or attached an Office communication concerning this application or proceeding.**

**Commissioner of Patents and Trademarks**

## Office Action Summary

| Application No. | Applicant(s) |
|---|---|
| 07/784,222 | WESTBROOK |
| **Examiner** | **Group Art Unit** |
| Dianne Rees | 1807 |

☒ Responsive to communication(s) filed on *Mar 29, 1995*.

☐ This action is **FINAL.**

☐ Since this application is in condition for allowance except for formal matters, **prosecution as to the merits is closed** in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11; 453 O.G. 213.

A shortened statutory period for response to this action is set to expire *3* month(s), or thirty days, whichever is longer, from the mailing date of this communication. Failure to respond within the period for response will cause the application to become abandoned. (35 U.S.C. § 133). Extensions of time may be obtained under the provisions of 37 CFR 1.136(a).

**Disposition of Claims**

☒ Claim(s) *1-30* is/are pending in the application.

Of the above, claim(s) _____ is/are withdrawn from consideration.

☐ Claim(s) _____ is/are allowed.

☒ Claim(s) *1-30* is/are rejected.

☐ Claim(s) _____ is/are objected to.

☐ Claims _____ are subject to restriction or election requirement.

**Application Papers**

☐ See the attached Notice of Draftsperson's Patent Drawing Review, PTO-948.

☐ The drawing(s) filed on _____ is/are objected to by the Examiner.

☐ The proposed drawing correction, filed on _____ is ☐ approved ☐ disapproved.

☐ The specification is objected to by the Examiner.

☐ The oath or declaration is objected to by the Examiner.

**Priority under 35 U.S.C. § 119**

☐ Acknowledgement is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d).

☐ All ☐ Some* ☐ None of the CERTIFIED copies of the priority documents have been

☐ received.

☐ received in Application No. (Series Code/Serial Number) _____.

☐ received in this national stage application from the International Bureau (PCT Rule 17.2(a)).

*Certified copies not received: _____.

☐ Acknowledgement is made of a claim for domestic priority under 35 U.S.C. § 119(e).

**Attachment(s)**

☒ Notice of References Cited, PTO-892

☐ Information Disclosure Statement(s), PTO-1449, Paper No(s). _____

☐ Interview Summary, PTO-413

☐ Notice of Draftsperson's Patent Drawing Review, PTO-948

☐ Notice of Informal Patent Application, PTO-152

*--- SEE OFFICE ACTION ON THE FOLLOWING PAGES ---*

**Part III DETAILED ACTION**

*Claim Rejections - 35 USC § 112*

1. Claims 1-30 are rejected under 35 U.S.C. § 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

The following phrases render the claims vague and indefinite:

a) In claim 1, the recitation of "contacting the probes with chromatin" in that it is unclear in what context this chromatin is present (as part of a chromosome? isolated? including or not including DNA?). The recitation of "homologous" further implies a very specific meaning of evolutionarily relatedness which the examiner is not sure that the claim intends (vs complementary with?). Clarification is requested. The recitation of the "probe sequences" is unclear as the claim has previously recited "probes" ; the claim might be amended to recite --sequences of the probes--. The recitation at step (c) of "detecting the presence of the probes" makes the claim further unclear as it is the detection of the hybridization of the probe which allows one to detect an aberration not just the presence of the probe. The

claim might be amended to recite --detecting said hybridization as a means of detecting the chromosome aberration--

b) In claim 4, the recitation of "the probes are further defined as at least approximately 800 kb apart" renders the claim indefinite in that it is not clear at what point in the method the probes are to be 800 kb apart. The claim might be amended to recite that the probes have the functional property of hybridizing to sequences that are approximately 800 kb apart in the aberrant chromosome.

c) In claim 6, the recitation of "wherein the fluorescent labels are microscopically distinct as different colors" renders the claim indefinite in that it is not clear how "microscopically distinct" is defined (distinguishable under a microscope as different colors?).

d) Claim 8 is indefinite in the recitation of "the chromatin probe contacts" as no chromatin probe contacts have been previously recited per se and thus the phrase lacks proper antecedent basis.

e) Claim 10 is indefinite in the recitation of "wherein the probes are juxtaposed in interphase", in that the probes themselves are not in interphase, the cells are (further the base claim previously recited that the cells are in interphase so this phrase seems redundant in claim 10). The claim is also indefinite in not reciting when during the method the probes are juxtaposed. The claim might be amended to recite --wherein the probes after

hybridization are juxtaposed as doublets if a chromosomal aberration is present--.

f) Claim 15 is indefinite in the recitation of "wherein the fusion gene is designated as p190" in that it is not clear how "designated" is defined in this claim (encodes?).

g) Claim 16 is indefinite in the recitation of PEM12, and MSB-1. These acronyms should be spelled out at least once in the claims or the probes identified by an appropriate SEQ. ID. No. for clarity.

h) Claim 17 is indefinite in the recitation of "wherein the cells comprise samples of human tissues" . It is unclear whether multiple different samples are provided (different tissues?different patients?). Clarification is requested,

i) Claim 21 is indefinite in the recitation of the "5'region of the major breakpoint cluster" as it is not clear what the metes and bounds of the "region" are (see also claim 22).

j) Claim 23 is in definite in that it is not clear what the metes and bounds of the probe are as it is not clear what sequences are encompassed by the term "3' end". The claim might be amended to recited the range of nucleotide sequences to which the probe hybridizes.

h) Claims 24-26 are indefinite over the recitation "wherein the probe comprises the designation PEM12 (or MSB-1, or c-H-able)" in that it is unclear how a probe can comprise a designation.

i) Claim 29 is indefinite in the recitation of "appropriate controls" in that it is not clear how "appropriate" is defined.

***Claim Rejections - 35 USC § 102***

2. The following is a quotation of the appropriate paragraphs of 35 U.S.C. § 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless --
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 1-14,16-20,22,23,24, and 26 are rejected under 35 U.S.C. § 102(b) as being anticipated by Gray et al. CA 2021489, 1/20/1990.

Gray et al. CA 2021489, 1/20/1990 teaches methods of detecting chromosomal aberrations using a plurality of chromosome probes and the use of this method to detect translocation such as those generating a BCR-ABL fusion and breakpoints associated with CML. The probes used are c-hu-ABL and PEM 12 (page 30) and the samples assayed are from cells at metaphase or interphase. The breakpoint regions detected in CML may be t(P;22)(q11:q34) (page 18). The method may involve the simultaneous detection of multiple loci in a genome comprising nucleic acid sequences that are substantially homologous to nucleic acid sequences in

multiple loci in a genome , wherein several to many clones of a sequence may be pooled (i.e a plurality of probes). Hybridization may be performed in situ. Test kits are also taught comprising high complexity probes for the detection of genetic rearrangements, and specifically for those producing the BCR-ABL fusion characteristic of CML. (page 23, , second to last paragraph, see also page 93).

Gray et al. also teaches that probes may be labelled with distinct labels to generate microscopically distinct colors (page 24) (see also Figure 10). Gray also teaches the use of biotinylated or digoxigenin labelled probes (page 70-71, page 108). Gray further teaches samples that are human lymphocytes (page 82, page 99)), (i.e such as from peripheral blood or bone marrow) and hamster-human hybrid cells (i.e cultured cells)(page 92).

3. The following is a quotation of the appropriate paragraphs of 35 U.S.C. § 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless --
> (a) the invention was known or used by others in this country, or patented or described in a printed publication in this or a foreign country, before the invention thereof by the applicant for a patent.

Claims 1-14,16-20,22,23,24, and 26 are rejected under 35 U.S.C. § 102(a) as being anticipated by Gray et al. EP 0 430 402

A2 (published 5/6/91). Gray et al. teaches the same methods and probes as discussed in paragraph 2.

*Claim Rejections - 35 USC § 103*

4. The following is a quotation of 35 U.S.C. § 103 which forms the basis for all obviousness rejections set forth in this Office action:

> A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.
>
> Subject matter developed by another person, which qualifies as prior art only under subsection (f) or (g) of section 102 of this title, shall not preclude patentability under this section where the subject matter and the claimed invention were, at the time the invention was made, owned by the same person or subject to an obligation of assignment to the same person.

Claims 1-30 are rejected under 35 U.S.C. § 103 as being unpatentable over Gray et al. in view of Bartram et al. (Blut 55:505-511,1987) and Biennerhassett et al. (Leukemia 2: 648-657, 1988)

Gray et al. meets all of the limitations of the claims except for the explicit teaching a genetic probe which is capable of hybridizing to the 5' region of the major breakpoint cluster region of chromosome 22, or to the first exon region of BCR, or a probe which is capable of recognizing the aberration that

produces p190. Gray also does not teach the provision of pairs of probes in a kit format.

However Bartram et al. teaches probes to the 5' part of the major breakpoint cluster (see abstract), and the use of this probes to detect different classes of translocation in CML. Biennerhassett further teaches a molecular characterization of the breakpoints that result in the production of p190 and teaches probes that hybridize to the first exon region (interpreted here as probes hybridizing to the intron between exons 1 and 2, and to be equivalent to a probe "designated as MSB-1"). It would therefor have been prima facie obvious to use the probes taught by Bartram and Biennerhassett in the method as taught by Gray for the expected benefit of being able to detect additional types of breakpoints and enhance the diagnostic utility of the assay. The inclusion of probe pairs in a kit would have been further prima facie obvious to one of ordinary skill in the art given the teachings of Gray et al. of the benefits of kits in general and the use of dual color fluorescence as an effective means of detecting chromosomal aberrations. One of ordinary skill in the art would have been motivated to put primer pairs in a kit for the expected benefit of providing a more rigorous diagnostic test with fewer false negatives.

***Double Patenting***

5. A rejection based on double patenting of the "same invention" type finds its support in the language of 35 U.S.C. 101 which states that "whoever invents or discovers any new and useful process ... may obtain a patent therefor ..." (Emphasis added). Thus, the term "same invention," in this context, means an invention drawn to identical subject matter. *Miller v. Eagle Mfg. Co.*, 151 U.S. 186 (1894); *In re Ockert*, 245 F.2d 467, 114 USPQ 330 (CCPA 1957); and *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970).

A statutory type (35 U.S.C. 101) double patenting rejection can be overcome by canceling or amending the conflicting claims so they are no longer coextensive in scope. The filing of a terminal disclaimer cannot overcome a double patenting rejection based upon 35 U.S.C. 101.

Claims 1-30 are provisionally rejected under 35 U.S.C. 101 as claiming the same invention as that of claims 1-30 of copending application Serial No. 08466781. This is a *provisional* double patenting rejection since the conflicting claims have not in fact been patented.

6. No claims are allowed.

7. Papers related to this application may be submitted to Group 1800 by facsimile transmission via the P.T.O. Fax Center located in Crystal Mall 1. The CM1 Fax Center number is (703) 305-7401. Please note that the faxing of such papers must conform with the notice to Comply published in the Official Gazette, 1096 OG 30 (Nov 15, 1989).

An inquiry regarding this communication should be directed to examiner Dianne Rees, Ph.D., whose telephone number is (703) 308-6565. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, W. Gary Jones, can be reached on (703) 308-1156.

Calls of a general nature may be directed to the Group receptionist who may be reached at (703) 308-0196.

Dianne Rees
6/2/96

W. GARY JONES
SUPERVISORY PATENT EXAMINER
GROUP 1800
6/2/96